REMARKS

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

I. Restriction requirement/election

Election, with traverse, of the claims of Group 13 (including claims 3, 9-14, and 23-27), drawn to polynucleotides encoding SEQ ID NO:14, polynucleotides of SEQ ID NO:29, vectors, host cells, and methods of using the polynucleotides to produce the encoded polypeptides, is acknowledged. Applicants thank the Examiner for rejoining claims drawn to polypeptides of SEQ ID NO:14 (including claim 1). Moreover, Applicants thank the Examiner for acknowledging that, upon allowance of the product claims, rejoinder of process claims commensurate in scope with the allowed product claims will be considered.

II. Objection to the specification

The Office Action objects to the specification because the application "does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required" (Office Action, September 3, 2003; page 4, § 2). However, Applicants believe that the requirement for an abstract **has** been met.

The M.P.E.P. directs Examiners to "[n]ote that the abstract for a national stage application filed under 35 U.S.C. 371 may be found on the front page of the Patent Cooperation Treaty publication (i.e., pamphlet). See MPEP § 1893.03(e)." M.P.E.P. § 608.01(b). The instant application is a national stage application under 35 U.S.C. § 371 of international patent application PCT/US99/23434, published on April 13, 2000 as international publication number WO 00/20604. An abstract was provided with the international patent application and was printed on the front cover of international publication number WO 00/20604. The provision of the abstract on the front cover of the international publication corresponding to the instant national stage application thus satisfies the requirement for an abstract.

For at least the above reasons, withdrawal of the objection to the specification is requested.

III. Objection to the claims

Claim 1 was objected to based on the allegation that it is "of improper dependent form for failing to further limit the subject matter of a previous claim" (Office Action, September 3, 2003; page 4, § 3). This objection is traversed.

Nevertheless, to expedite prosecution, claim 1 has been rewritten in independent form, as suggested by the Examiner. Therefore, withdrawal of this objection is requested.

IV. Written description rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 5, 9, 11-14, 23, 24, and 26 were rejected under 35 U.S.C. § 112, first paragraph, as being based on a specification which allegedly fails to reasonably convey to one of skill in the art that the Applicants had possession of the claimed invention at the time the application was filed. The Office Action asserts that "the written description is not commensurate in scope with the claims drawn to 'naturally occurring' polynucleotide variants encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14" (Office Action, September 3, 2003; page 5), and that "[s]ince the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, nucleic acid molecules comprising at least 60 contiguous nucleotides of SEQ ID NO:29 alone are insufficient to describe the genus" (Office Action, September 3, 2003; pages 7-8). This rejection is traversed.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*
> *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. [footnotes omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

A. The specification provides an adequate written description of the claimed "variants" and "fragments" of SEQ ID NO:14 and SEQ ID NO:29.

The subject matter encompassed by claims 1, 3, 5, 9, 11-14, 23, 24, and 26 is either disclosed by the specification or is conventional or well known to one skilled in the art.

First note that the "variant" language of independent claim 3 recites a polynucleotide encoding "a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to" the amino acid sequence of SEQ ID NO:14 and the "variant" language of independent claim 9 recites "a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to" the polynucleotide sequence of SEQ ID NO:29. Furthermore, the "fragment" language of independent claim 11 recites a polynucleotide "comprising at least 60 contiguous nucleotides" of a polynucleotide comprising SEQ ID NO:29, or of a polynucleotide "comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:29."

The amino acid sequence of SEQ ID NO:14 and the polynucleotide sequence of SEQ ID NO:29 are explicitly disclosed in the specification. See, for example, the Sequence Listing. Variants of SEQ ID NO:14 and SEQ ID NO:29 are described in the Specification at, for example, page 5, lines 23-30; page 6, lines 11-16; page 8, line15 to page 9, line 2; page 15, lines 3-22; page 16, lines 24-27; and page 16, line 31 to page 17, line 14. Fragments of SEQ ID NO:14 and SEQ ID NO:29 are described in the Specification at, for example, page 5, line 20 to page 6, line 2; page 6, lines 9-16; page

9, lines 3-8; page 10, lines 6-9; page 13, lines 8-18 and 25-29; page 16, lines 20-23; page 17, lines 25-29; page 26, lines 2-7; page 30, lines 9-15; page 42, lines 6-7; page 43, lines 10-12; page 49, lines 2-13 and 29-34; page 50, lines 6-9; and page 53, lines 3-6. In addition, assays to measure pyrroline-5-carboxylate reductase activity are known in the art (See, for example, page 9353 of Merrill et al., J. Biol. Chem., 1989, 264:9352-9358; of record).

One of ordinary skill in the art would recognize polynucleotide sequences which are variants having a polynucleotide sequence at least 90% identical to SEQ ID NO:29, or which encode polypeptide variants having an amino acid sequence at least 90% identical to SEQ ID NO:14. Given any naturally occurring polynucleotide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:29, or whether it encoded a variant of SEQ ID NO:14. It would also be routine to determine whether such a variant had pyrroline-5-carboxylate reductase activity, using assays known in the art. Accordingly, the specification provides an adequate written description of the recited polynucleotide variants of SEQ ID NO:29 and polynucleotides encoding polypeptide variants of SEQ ID NO:14.

One of ordinary skill in the art would recognize polynucleotide sequences which are fragments comprising at least 60 contiguous nucleotides of SEQ ID NO:29, or comprising at least 60 contiguous nucleotides of variants of SEQ ID NO:29. The information provided by SEQ ID NO:29 provides the necessary framework for the recited fragments -- to recite every possible fragment would needlessly clutter the application. Furthermore, since there is an adequate written description of the recited variants of SEQ ID NO:29 (as discussed above), the variants of SEQ ID NO:29 provide the necessary framework for the recited fragments of these variants. Accordingly, the specification provides an adequate written description of the recited polynucleotide fragments of SEQ ID NO:29, and of the recited polynucleotide fragments of variants of SEQ ID NO:29.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of

such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. § 112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides and polypeptides in terms of chemical structure, rather than functional characteristics. For example, the language of independent claims 3 and 9 recites chemical structure to define the claimed genus:

> 3. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:
> a) a polypeptide comprising [the amino acid sequence of SEQ ID NO:14],
> b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to [the amino acid sequence of SEQ ID NO:14],
> c) a fragment of a polypeptide having [the amino acid sequence of SEQ ID NO:14], wherein the fragment has oxidoreductase activity, and
> d) an immunogenic fragment comprising at least 10 contiguous amino acid residues of a polypeptide having [the amino acid sequence of SEQ ID NO:14].
>
> 9. An isolated polynucleotide selected from the group consisting of:
> a) a polynucleotide comprising [the polynucleotide sequence of SEQ ID NO:29],
> b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to [the polynucleotide sequence of SEQ ID NO:29],
> c) a polynucleotide complementary to a polynucleotide of a),
> d) a polynucleotide complementary to a polynucleotide of b), and
> e) an RNA equivalent of a)-d).

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:14 and SEQ ID NO:29. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides and polypeptides. The polynucleotides and polypeptides defined by the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base the written description inquiry "on whatever is now claimed," the Patent Office failed to

provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

The Patent Office Guidelines indicate that evidence that Applicants were in possession of the claimed invention can include "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, **or** some combination of such characteristics" (P.T.O. Guidelines, *supra*; emphasis added). The claimed polynucleotides and polypeptides have been described by chemical structure (e.g., relation of the recited polynucleotides to SEQ ID NO:29, relation of the recited polypeptides to SEQ ID NO:14), physical properties (e.g., occurrence in nature of the recited variant sequences), and chemical properties (e.g., possession of pyrroline-5-carboxylate reductase activity, oxidoreductase activity and/or immunogenic activity). Therefore, the written description requirement has been met.

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that, rather than being a large variable genus, the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA, 1998, 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues (Brenner et al., pages 6073 and 6076). Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins (Brenner et al., page 6076).

The present application is directed, *inter alia*, to polynucleotides encoding oxidoreductase proteins and to polypeptides which are oxidoreductase proteins, including oxidoreductase proteins related to the amino acid sequence of SEQ ID NO:14. In accordance with Brenner et al., naturally

occurring molecules may exist which could be characterized as oxidoreductase proteins and which have as little as 30% identity over at least 150 residues to SEQ ID NO:14. The "variant language" of the present claims recites a polynucleotide encoding "a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to" the amino acid sequence of SEQ ID NO:14 (note that SEQ ID NO:14 has 274 amino acid residues). This variation is far less than that of polynucleotides encoding all potential oxidoreductase proteins related to SEQ ID NO:14, i.e., those oxidoreductase proteins having as little as 30% identity over at least 150 residues to SEQ ID NO:14.

The Office Action asserts that the genus of recited polynucleotide fragments is highly variant because "a significant number of structural differences between genus members is permitted" (Office Action, September 3, 2003; page 7). To the contrary. The genus of recited polynucleotide fragments is not highly variant because the members of the genus are defined within the structural framework of the polynucleotide sequence of SEQ ID NO:29, or of the recited naturally occurring variants of SEQ ID NO:29.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. § 112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those cases was based on the state of the art at essentially the "dark ages" of recombinant DNA technology.

The present application is a U.S. national stage application of international patent application PCT/US99/23434, filed October 6, 1999, which claims the benefit of priority of U.S. provisional patent applications filed between October, 1998 and March, 1999. Much has happened in the development of recombinant DNA technology in the 20 or so years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been

compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO:14 and SEQ ID NO:29, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide and polypeptide variants and fragments, and polynucleotides encoding the recited polypeptide variants and fragments, at the time of filing of this application.

4. Summary

The Office Action failed to base the written description inquiry "on whatever is now claimed." Consequently, the Office Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:14 and SEQ ID NO:29. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

For at least the reasons set forth above, the specification provides an adequate written description of the claimed subject matter, and this rejection should be withdrawn.

V. Enablement rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 9, 11-14, and 26-27 were rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the specification does not describe the subject matter of the invention in such a way as to enable one of skill in the art to make and/or use the claimed variants and fragments. In particular, the Office Action asserts that the specification does not enable a skilled artisan to make and use "a polynucleotide comprising at least 60 nucleotides of SEQ ID NO:29 as recited in claim 11"

(Office Action, September 3, 2003; page 8), or "an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence at least 90% amino acid sequence identity to SEQ ID NO:14" (Office Action, September 3, 2003; page 9). Such, however, is not the case.

With respect to the claimed fragments, the Office Action asserts that "[t]he claimed genus of polynucleotide molecules encompasses variants that do not share activity of the polypeptide" (Office Action, September 3, 2003; page 8). However, it is not necessary for a polynucleotide fragment to share the activity of the SEQ ID NO:14 polypeptide in order for one of skill in the art to be able to use that polynucleotide fragment without undue experimentation. One of skill in the art could make and use the claimed polynucleotide fragments without undue experimentation, based on the specification and the state of the art at the time the application was filed. For example, one of skill in the art would know how to use the claimed polynucleotide fragments as hybridization probes or PCR probes to detect the presence of a polynucleotide comprising SEQ ID NO:29 (Specification, e.g., at page 17, line 30 to page 18, line 28; page 37, line 26 to page 38, line 3; and Example VI at page 49). Since a skilled artisan would know how to make the claimed polynucleotide fragments, and use them as hybridization probes and/or PCR probes, the Office Action's assertion that the specification "is not enabled for a nucleic acid molecule of nucleotide sequence anything less than what is disclosed in SEQ ID NO:29" (Office Action, September 3, 2003; page 8) is incorrect.

With respect to the claimed variants, the Office Action asserts that "[t]here is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a polypeptide other than that exemplified in the specification" (Office Action, September 3, 2003; page 9). Note that claim 3, for example, recites not only that the polynucleotides encode polypeptide variants which are at least 90% identical to SEQ ID NO:14, but also that they have "**a naturally occurring amino acid sequence**." Through the process of natural selection, nature will have determined the appropriate amino acid sequences. Given the information provided by SEQ ID NO:14 (the amino acid sequence of OXRE-14) and SEQ ID NO:29 (the polynucleotide sequence

encoding OXRE-14), one of skill in the art would be able to routinely obtain "a naturally occurring amino acid sequence at least 90% identical to" the amino acid sequence of SEQ ID NO:14.

For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the specification of the instant application. See, e.g., page 17, line 30 to page 18, line 28; page 37, line 26 to page 38, line 3; and Example VI at page 49. Thus, one skilled in the art need not make and test vast numbers of polynucleotides that encode polypeptides based on the amino acid sequence of SEQ ID NO:14, or vast numbers of polynucleotides based on the polynucleotide sequence of SEQ ID NO:29. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides, and their encoded polypeptides, that already exist in nature. By adjusting the nature of the probes or nucleic acids (i.e., non-conserved, conserved, or highly conserved) and the conditions of hybridization (maximum, high, intermediate, or low stringency), one can obtain variant polynucleotides of SEQ ID NO:29 which, in turn, will allow one to make the variant polypeptides of SEQ ID NO:14 recited by the present claims using conventional techniques of recombinant protein production. By extension, one of skill in art could make fragments of naturally occurring polynucleotides at least 90% identical to SEQ ID NO:29, and could use such fragments, for example, as hybridization probes to detect full-length naturally occuring polynucleotides at least 90% identical to SEQ ID NO:29. Similarly, a skilled artisan could make polynucleotides encoding fragments of the SEQ ID NO:14 polypeptide, and could use such fragments, for example, as hybridization probes to detect polynucleotides encoding full-length human variants of the SEQ ID NO:14 polypeptide.

Furthermore, the Office Action asserts that "no guidance is provided as to which of the myriad of polynucleotide species encoding polypeptide species encompassed by the claim will retain the desired characteristics" (Office Action, September 3, 2003; page 9). However, it is not necessary to provide polynucleotides which retain the functional characteristics of the SEQ ID NO:14 polypeptide in order to make and/or use the recited polynucleotide variants and fragments. The activity and functional characteristics of polypeptides encoded by the recited polynucleotide fragments and variants has no bearing on the ability of a skilled artisan to screen a cDNA library or use appropriate PCR conditions

to identify relevant polynucleotides, and their encoded polypeptides, that already exist in nature, without undue experimentation. Moreover, it is irrelevant whether any of the claimed polynucleotides encode polypeptide variants which have any biological functions at all. One of skill in the art would still know how to make and use such polynucleotides, without undue experimentation. For example, polynucleotides which encode nonfunctional polypeptide variants of SEQ ID NO:14 could be used to detect polynucleotides which encode the polypeptide of SEQ ID NO:14 by, for example, hybridization and/or PCR techniques. It is not necessary for a polynucleotide to encode a functional polypeptide for one of skill in the art to be able to use that polynucleotide without undue experimentation.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Office Action has failed to provide any **reasons** why one would doubt that the guidance provided by the present Specification would enable one to make and use the recited polynucleotide variants and fragments. Hence, a *prima facie* case for non-enablement has not been established with respect to the recited polynucleotide variants and fragments.

For at least the above reasons, withdrawal of these rejections is requested.

VI. Rejection of claims 1, 3-5, 9-10, and 12-14 under 35 U.S.C. § 112, second paragraph

Claims 1, 3-5, 9-10, and 12-14 were rejected under 35 U.S.C. § 112, second paragraph, based on the allegation that the recitation of non-elected subject matter is vague and indefinite. This rejection is traversed.

According to the M.P.E.P., there are two separate requirements set forth in the second paragraph of 35 U.S.C. § 112:

> (A) the claims must set forth the subject matter that applicants regard as their invention; and
>
> (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. M.P.E.P. § 2171.

The present claims satisfy both of these requirements.

SEQ ID NO:29 was provisionally elected for examination in the Response to Restriction Requirement of June 16, 2003. However, Applicants have traversed the Restriction Requirement, and regard their invention as including all of the polynucleotides and polypeptides recited by the claims. It is believed that upon searching and examining SEQ ID NO:29 and finding no prior art over which SEQ ID NO:29 can be rejected, the search should be extended to include SEQ ID NO:16-28 and SEQ ID NO:30, the non-elected species. Thus, the claims set forth the subject matter that Applicants regard as their invention.

Furthermore, one of ordinary skill in the art would reasonably understand the metes and bounds of the claimed subject matter, even if that subject matter encompasses polynucleotides and polypeptides having sequences which are currently not under examination. The ability of a skilled artisan to understand the metes and bounds of claimed subject matter is not affected by whether that subject matter is elected or not.

For at least the above reasons, the claims meet the requirements of 35 U.S.C. § 112, second paragraph, and withdrawal of these rejections is requested.

VII. Rejection of claims 3, 9, 23, 24, and 26 under 35 U.S.C. § 112, second paragraph

Claims 3, 9, 23, 24, and 26 were rejected under 35 U.S.C. § 112, second paragraph, based on the allegation that the recitation of "naturally occurring" is indefinite. The Office Action asserts that "[i]t is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, nucleic acid molecules amplified from cDNA or all nucleic acid molecules that encode the polypeptide" (Office Action, September 3, 2003; page 10). This rejection is traversed.

Under the second paragraph of 35 U.S.C. § 112, the standard for "definiteness" is that the claims define patentable subject matter with a **reasonable** degree of precision and particularity. See *In re Miller*, 169 USPQ 597, 599 (CCPA 1971); *In re Moore*, 169 USPQ 236, 238 (CCPA 1971). See also M.P.E.P. § 706.03(d). In this regard, the Supreme Court has indicated that the primary purpose of claim language is to give "fair" notice of what would constitute the infringement of a claim. See *United Carbon Co. v. Binny & Smith Co.*, 317 U.S. 228, 55 USPQ 381 (1942). In other words, the basic purpose of 35 U.S.C. § 112, second paragraph is to require a claim to reasonably apprise those skilled in the art of the scope of the invention defined by that claim and give fair notice of what constitutes infringement of the claim. See *Antonius v. Pro Group Inc.*, 217 USPQ 875, 877 (6th Cir.1983). The present claims meet the legal standards required by 35 U.S.C. § 112, second paragraph.

The term "naturally occurring" is not a limitation of the claimed polynucleotides themselves, as the Office Action seems to imply. This term is a limitation of the **polynucleotide sequences** comprised by the claimed polynucleotides and of the **amino acid sequences** comprised by the recited polypeptides encoded by the claimed polynucleotides. For example, the "variant" language of claim 3 recites an isolated polynucleotide encoding "a polypeptide comprising a **naturally occurring amino acid sequence** at least 90% identical to" the amino acid sequence of SEQ ID NO:14. Similarly, the "variant" language of claim 9 recites an isolated polynucleotide "comprising a **naturally occurring polynucleotide sequence** at least 90% identical to" the polynucleotide sequence of SEQ ID NO:29. The term "naturally occurring," in the context of polynucleotide and amino acid sequences, is supported in the specification at, for example, page 8, lines 8-11 and 15-21; page 15, lines 11-22; page 17, lines 15-19; page 37, line 26 to page 38, line 3; and page 60, lines 6-7. One of skill in the art would reasonably understand that the recitation of "naturally occurring" sequences encompasses any sequence which occurs in nature.

Furthermore, one of skill in the art would reasonably understand, based on the language of the claims, that the claimed isolated polynucleotides are not naturally occurring; they are actual physical molecules which can be made by man. For example, the claimed isolated polynucleotides could be isolated from a natural source, they could be amplified by PCR from a natural source, they could be

produced by recombinant DNA techniques, or they could be chemically synthesized *de novo*. The chemical structures of these man-made polynucleotides are based on the information provided by the naturally occurring amino acid sequence of SEQ ID NO:14, and the naturally occurring polynucleotide sequence of SEQ ID NO:29. Therefore, the claims are definite in their recitation of isolated, man-made polynucleotides which have sequences derived from naturally occurring molecules.

For at least the above reasons, withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is requested.

VIII. Rejection of claim 5 under 35 U.S.C. § 112, second paragraph

Claim 5 was rejected under 35 U.S.C. § 112, second paragraph, based on the allegation that the recitation of the phrase "hybridizes" is indefinite. The Office Action asserts that the recitation of hybridization conditions "renders the claim vague and indefinite because it is not the hybridization conditions but the wash conditions that are important in determining whether the matches between the polynucleotide molecules are perfect or imperfect" (Office Action, September 3, 2003; page 11). This rejection is traversed.

To expedite prosecution, claim 5 has been canceled, without prejudice or disclaimer. By this amendment, Applicants expressly do not disclaim equivalents of the invention which could include polynucleotides which hybridize to the claimed polynucleotides under any hybridization and/or wash conditions. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the instant application. While not conceding to the Patent Office position, it is believed that the rejection as it applies to canceled claim 5 is moot. Therefore, withdrawal of this rejection is requested.

IX. Rejection of claims 3 and 23 under 35 U.S.C. § 112, second paragraph

Claims 3 and 23 were rejected under 35 U.S.C. § 112, second paragraph, based on the allegation that the recitation of the phrase "immunogenic fragment" is indefinite. The Office Action asserts that "[i]t is unclear what the metes and bounds of this term are" (Office Action, September 3, 2003; page 11). This rejection is traversed.

To expedite prosecution, claims 3 and 23 have been amended such that the recited immunogenic fragments comprise "at least 10 contiguous amino acid residues" of the amino acid sequence of SEQ ID NO:14. Support for these amendments can be found in the specification at, for example, page 30, lines 9-11. By these amendments, Applicants expressly do not disclaim equivalents of the invention which could include polypeptides comprising immunogenic fragments comprising fewer than 10 contiguous amino acid residues of SEQ ID NO:14, or polynucleotides encoding immunogenic fragments comprising fewer than 10 contiguous amino acid residues of SEQ ID NO:14. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the instant application. While not conceding to the Patent Office position, it is believed that claims 3 and 23, as amended, recite patentable subject matter.

For at least the above reasons, withdrawal of these rejections is requested.

X. Rejection of claims 24, 26, and 27 under 35 U.S.C. § 112, second paragraph

Claims 24, 26, and 27 were rejected under 35 U.S.C. § 112, second paragraph, because they allegedly "depend on the above rejected claims for their limitations" (Office Action, September 3, 2003; page 11). This rejection is traversed.

The rejection of claims 24 and 26 under 35 U.S.C. § 112, second paragraph, has been addressed above, in the discussion of the rejection of claims 3, 9, 23, 24, and 26 under 35 U.S.C. § 112, second paragraph, for the recitation of the term "naturally occurring" (e.g., in § VII). For at least the above reasons, this rejection of claims 24 and 26 should be withdrawn.

With respect to this rejection, claim 27 is directed to inventions defined by SEQ ID NO:29. The Office Action's rejection is based on the alleged indefiniteness of claims drawn to non-elected subject matter, claims reciting the term "naturally occurring," claims reciting the term "hybridizes," and claims reciting the term "immunogenic fragment." Thus, this rejection should not apply to claim 27. For at least this reason, this rejection of claim 27 should be withdrawn.

XI. Rejections under 35 U.S.C. § 102(a)

Claims 1, 3, 5, and 23 were rejected under 35 U.S.C. § 102(a) because the recited immunogenic fragments of SEQ ID NO:1 are allegedly anticipated by Dougherty et al. (J. Biol. Chem., 1992, 267:871-875). The Office Action asserts that "an immunogenic fragment of the polypeptide of the reference, would potentially be any six amino acids . . . the polynucleotide of the reference would potentially be capable of hybridizing to the polynucleotide of SEQ ID NO:29 . . . [t]herefore, the cDNA and polypeptide disclosed in the reference meets the limitations of claims 1, 3, 5, 23" (Office Action, September 3, 2003; pages 11-12). This rejection is traversed.

To expedite prosecution, claim 5 has been canceled, without prejudice or disclaimer. Furthermore, claims 1, 3, and 23 have been amended such that the recited immunogenic fragments comprise "at least 10 contiguous amino acid residues" of the amino acid sequence of SEQ ID NO:14. Support for these amendments can be found in the specification at, for example, page 30, lines 9-11. By these amendments, Applicants expressly do not disclaim equivalents of the invention which could include polypeptides comprising immunogenic fragments comprising fewer than 10 contiguous amino acid residues of SEQ ID NO:14, polynucleotides encoding immunogenic fragments comprising fewer than 10 contiguous amino acid residues of SEQ ID NO:14, or polynucleotides which hybridize to the claimed polynucleotides under any hybridization and/or wash conditions. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the instant application. While not conceding to the Patent Office position, it is believed that claims 1, 3, and 23, as amended, recite patentable subject matter. Furthermore, with respect to canceled claim 5, the rejection is moot. Therefore, withdrawal of these rejections is requested.

XII. Allowable subject matter

Applicants thank the Examiner for indicating that claim 25 would be allowable if rewritten in independent form (See pages 1 and 12 of the Office Action of September 3, 2003). Applicants believe that the base claims recite patentable subject matter, so withdrawal of this objection is requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at (650) 621-8581.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**.

Respectfully submitted,

INCYTE CORPORATION

Date: December 3, 2003

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Limited Recognition (37 C.F.R. § 10.9(b)) attached
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